REMARKS

Reconsideration is respectfully requested. Claims 11-25 are pending. Claims 14-16 and 19 are withdrawn. The specification and claims 11 and 25 have been amended.

Support for the amendment to the specification can be found on page 33, first full paragraph, and in the references cited therein and incorporated by reference, particularly PCT/US98/12082.

Support for the amendment to claims 11 and 25 can be found, for example, in the claims as originally filed, in the last paragraph on page 4 of the specification and in the first paragraph of page 105 of the specification.

Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Claim Rejections – 35 USC 112

Claims 13 and 20 stand rejected under 35 USC 112, first paragraph, for allegedly failing to comply with the written description requirement. This is a new matter rejection. Applicants respectfully traverse.

Claim 13

Claim 13 recites "applying the output waveform to a digital lock-in amplifier."

The specification discloses that "suitable 'output' AC techniques include. . . bandwidth narrowing techniques [,]including lock-in detection schemes" page 4, last paragraph, and "[t]he response from an electrochemical cell can be processed with a lock-in amplifier[,]" page 104, first paragraph.

Example 2 describes a reduction to practice in which a digital lock-in amplifier was used. The first paragraph of page 123 discloses that "[t]he transconductance amplifier was equipped with summing circuitry that combines a DC ramp from the computer DAQ card and an AC sine wave from the lock-in amplifier (SR830 Stanford Instruments)." The SR830 lock-in amplifier is a digital lock-in amplifier as shown in the SR830 product datasheet attached as Exhibit A and entitled "Digital Lock-In Amplifiers: SR810 and SR830 – DSP lock-in amplifiers." According to page 1, paragraph 1 of the SR830 datasheet, the SR830 uses "digital signal processing (DSP)[.]" Page 2, paragraph 1 of the product datasheet states that

> Conventional lock-in amplifiers use an analog demodulator to mix an input signal with a reference signal. . . . Demodulation in the SR810 and SR830 is accomplished by sampling the input signal with a high-precision A/D converter, and multiplying the digitized input by a synthesized reference signal. This digital demodulation technique results in more than 100 dB of true dynamic reserve (no prefiltering) and is free of the errors associated with analog instruments.

Thus, by referencing the SR830 digital lock-in amplifier that was used in an actual reduction to practice, the specification discloses "a digital lock-in amplifier" as claimed. Applicants note that "there is no *in haec verba* requirement" and that claim limitations can be supported "through express, implicit, or inherent disclosure." MPEP 2163(I)(B). Actual reduction to practice is sufficient to show the possession that is necessary to satisfy the written description requirement. MPEP 2163(I). Accordingly, Applicants respectfully request withdrawal of this rejection.

Claim 20

Claim 20 recites that "the input waveform comprises at least a portion having a frequency of about 100 kHz."

The instant specification on page 33, first full paragraph, properly incorporates by reference PCT/US98/12082. Lines 16 to 26 of page 28 of PCT/US98/12082 discloses characteristics of the input waveform that can be used to initiate electron transfer. Applicants have amended the last paragraph of page 92 of

the instant specification by inserting lines 24 to 26 of page 28 of PCT/US98/12082, which states that the frequency range "from about 1 Hz to about 100 kHz" is "especially preferred." The instant application as amended thus provides support for the limitation in claim 20 in which "the input waveform comprises at least a portion having a frequency of about 100 kHz."

Because the instant application provides support for all the limitations recited in claims 13 and 20, the new matter rejection is improper and should be withdrawn.

<u>Claims 11-13, 17, 18 and 20-25</u>

Claims 11-13, 17, 18 and 20-25 stand rejected under 35 USC 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. Specifically, the Examiner alleges that claims 11 and 25 are vague and indefinite, stating

> Since the claim does not indicate how difference between the output waveform of an array complex in the presence of a target analyte and the output waveform of an array complex in the absence of the target analysis, it is unclear how analyzing the output waveform of an array complex in the presence of a target analyte can be used as an indication of the presence of a target analyte.

Applicants respectfully traverse.

Claim 11 recites "analyzing the output waveform for the presence of the characteristic waveform as an indication of the presence of said target analytes." The specification discloses on page 92, second paragraph from the bottom, that

> Accordingly, when using AC initiation and detection methods, the frequency response of the system changes as a result of the presence of the ETM. By "frequency response" herein is meant a modification of signals as a result of electron transfer between the electrode and the ETM.

The specification further discloses on page 94, second full paragraph, that:

> In one embodiment, detection utilizes a single measurement of output signal at a single frequency. That is, the frequency response of the system in the absence of target sequence, and thus the absence of label probe containing ETMs, can be previously determined to be very low at a particular high frequency. Using this information, any response at a particular frequency, will show the presence of the assay complex. That is, any response at a particular frequency is characteristic of the assay complex. Thus, it may only be necessary to use a single input frequency, and any changes in frequency response is an indication that the ETM is present, and thus that the target sequence is present.

As disclosed by the specification, the frequency response of the system in the absence of a target is very low at particular frequencies. Therefore, "any response at a particular frequency will show the presence of the assay complex." In this way, by "analyzing the output waveform for the presence of the characteristic waveform" according to claim 11, one can obtain "an indication of the presence of said target analytes." As such, claim 11 and claims dependent therefrom are not indefinite.

In claim 25, the assay complex comprises "a target analyte, a capture binding ligand and an electron transfer moiety." The capture binding ligand serves to anchor the target analytes to the electrode surface. Specification, p. 5, ¶ 2. "[T]he presence of the ETM near the electrode surface is dependent on the presence of the target analyte." *Id.* Electron transfer can then be initiated between the ETM and the electrode. "[B]y detecting electron transfer, the presence or absence of the target analyte is determined." *Id.* Chronocoulometry, as recited in claim 25, is merely one type of analysis that can be applied to the output waveform to detect electronic transfer. *Id.* at p. 101, ¶ 1. Since detecting electron transfer through chronocoulometry provides an indication of the presence of target analytes, claim 25 is not indefinite.

For the forgoing reasons claims 11-13, 17, 18 and 20-25 are not indefinite. Applicants request that the Examiner withdraw this rejection.

Claim Rejections – 35 USC 102

Claims 11-13, 17, 18, 20, 21, 24 and 25 stand under 35 USC 102(e) as allegedly being anticipated by US Patent 6,013,459 to Meade ("*Meade*"). Applicants respectfully traverse.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." MPEP 2131.

Independent claims 11 and 25 have been amended such that analyzing the output waveform comprises peak recognition. *Meade* does not explicitly teach analyzing an output waveform using peak recognition. Because *Meade* does not explicitly teach each and every element of independent claims 11 and 25 as amended, *Meade* does not anticipate claims 11-13, 17, 18, 20, 21, 24 and 25. Applicants therefore respectfully request withdrawal of the rejection.

Claim Rejections – 35 USC 103

Claims 22 and 23 stand rejected under 35 USC 103(a) as allegedly being unpatentable over *Meade* in view of US Patent 5,487,032 to Mihara et al. ("*Mihara*").

Under 35 USC 103(c)(1), *Meade* cannot preclude patentability of the presently claimed invention under 35 USC 103.

35 USC 103(c)(1) states that

> Subject matter developed by another person, which qualifies as prior art only under one or more of subsections (e), (f), and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the claimed invention was made, owned by the same person or subject to an obligation of assignment to the same person.

1. *Meade* is not a prior art reference under 35 USC 102(a), (b), (c), or (d), and so could only be alleged prior art under 35 USC 102(e), (f), or (g).

The instant application claims priority to US Application No. 60/100,730 filed on September 17, 1998. *Meade* was published January 11, 2000, after the effective filing date of the instant application, and thus could qualify as prior art only under 35 USC 102(e), (f), or (g).

2. Statement of Common Ownership.

In accordance with the requirements to establish common ownership articulated in MPEP 706.02(l)(2), the instant US Patent Application No. 10/714,489 and the *Meade* patent were, at the time the invention of the instant application was made, owned by Clinical Micro Sensors, Inc.

Applicants respectfully note that "**[t]his statement alone is sufficient evidence** to disqualify [the patent] from being used in a rejection under 35 U.S.C. 103(a) against the claims of [the instant application]." MPEP 706.02(l)(2)(II). In the rare instance that the Examiner has independent evidence that raises material doubt as to the accuracy of applicant's representation of common ownership, the Examiner needs to "explain why the accuracy of the representation is doubted." *Id.*

The Examiner has provided absolutely no reasonable basis for doubting the accuracy of Applicant's representation of common ownership. Although the statement of common ownership provided in Applicants' previously filed response "alone" should have been sufficient evidence, Applicants also made reference to the reel and frame numbers of the recorded assignment in *Meade* as well as the recorded assignment in US Patent Application No. 09/397,957 (now US Patent No. 6,740,518), which is a parent of the instant application. Such "reference to assignments recorded in the U.S. Patent and Trademark Office in accordance with 37 CFR Part 3 which convey the entire rights in the applications to the same person(s) or organization(s)" is the "objective evidence" that the Examiner claims is lacking. *See* MPEP 706.02(l)(2)(II). Furthermore, although "the examiner cannot locate an assignment of this instant case," Applicants note that "[i]n the case of a division or continuation application, a prior assignment recorded against the original application is applied (effective) to the division or continuation application because the assignment

recorded against the original application gives the assignee rights to the subject matter common to both applications." MPEP 306. Since the instant application is a continuation of US Application No. 09/397,957 (*see* Specification, p. 1, ¶ 1) and assignments of the subject matter to Clinical Micro Sensors, Inc. were executed and recorded in that case, the present subject matter is also assigned to Clinical Micro Sensors, Inc.

Therefore, *Meade* cannot preclude patentability of the presently claimed invention under 35 USC 103. Because this ground for rejection is improper, Applicants respectfully request that it be withdrawn.

CONCLUSION

Applicants believe the claims are in a condition for allowance. Early notification thereof is respectfully requested. The Examiner is invited to call the undersigned at 415.442.1000 to resolve any questions. Although Applicants do not believe any additional fees are required, the Commissioner is authorized to charge any additional fees that may be required or to credit any overpayment to Deposit Account No. 50-0310 (Docket No. 067456-5012US02).

Respectfully submitted,
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Robin M. Silva

Robin M. Silva, Reg. No. 38,304

Dated: 10/30/07

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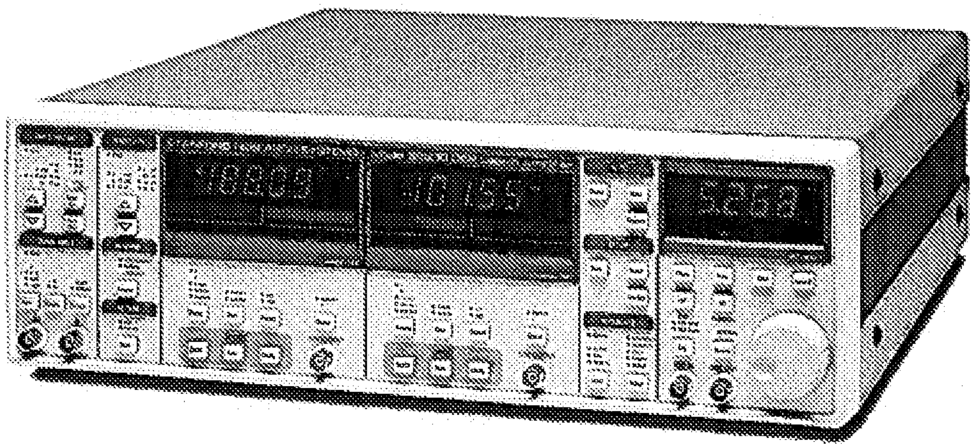
Digital Lock-In Amplifiers

SR810 and SR830 — DSP lock-in amplifiers



SR830 DSP Lock-In Amplifier

SR810 & SR830 DSP Lock-In Amplifiers —

- **1 mHz to 102.4 kHz frequency range**
- **>100 dB dynamic reserve**
- **5 ppm/°C stability**
- **0.01 degree phase resolution**
- **Time constants from 10 µs to 30 ks (up to 24 dB/oct rolloff)**
- **Auto-gain, -phase, -reserve and -offset**
- **Synthesized reference source**
- **GPIB and RS-232 interfaces**

- **SR810 ... $3850** *(U.S. list)*
- **SR830 ... $4500** *(U.S. list)*

The SR810 and SR830 DSP Lock-In Amplifiers provide high performance at a reasonable cost. The SR830 simultaneously displays the magnitude and phase of a signal, while the SR810 displays the magnitude only. Both instruments use digital signal processing (DSP) to replace the demodulators, output filters, and amplifiers found in conventional lock-ins. The SR810 and SR830 provide uncompromised performance with an operating range of 1 mHz to 102 kHz and 100 dB of drift-free dynamic reserve.

Input Channel

The SR810 and SR830 have differential inputs with 6 nV/√Hz input noise. The input impedance is 10 MΩ, and minimum full-scale input voltage sensitivity is 2 nV. The inputs can also be configured for current measurements with selectable current gains of 10^6 and 10^8 V/A. A line filter (50 Hz or 60 Hz) and a 2× line filter (100 Hz or 120 Hz) are provided to eliminate line related interference. However, unlike conventional lock-in amplifiers, no tracking band-pass filter is needed at the input. This filter is used by conventional lock-ins to increase dynamic reserve. Unfortunately, band pass filters also introduce noise, amplitude and phase error, and drift. The DSP design of these lock-ins has such inherently large dynamic reserve that no band pass filter is needed.

Extended Dynamic Reserve

The dynamic reserve of a lock-in amplifier, at a given full-scale input voltage, is the ratio (in dB) of the largest interfering

signal to the full-scale input voltage. The largest interfering signal is defined as the amplitude of the largest signal at any frequency that can be applied to the input before the lock-in cannot measure a signal with its specified accuracy.

Conventional lock-in amplifiers use an analog demodulator to mix an input signal with a reference signal. Dynamic reserve is limited to about 60 dB, and these instruments suffer from poor stability, output drift, and excessive gain and phase error. Demodulation in the SR810 and SR830 is accomplished by sampling the input signal with a high-precision A/D converter, and multiplying the digitized input by a synthesized reference signal. This digital demodulation technique results in more than 100 dB of true dynamic reserve (no prefiltering) and is free of the errors associated with analog instruments.

Digital Filtering

The digital signal processor also handles the task of output filtering, allowing time constants from 10 µs to 30,000 s with a choice of 6, 12, 18 and 24 dB/oct rolloff. For low frequency measurements (below 200 Hz), synchronous filters can be engaged to notch out multiples of the reference frequency. Since the harmonics of the reference have been eliminated (notably 2F), effective output filtering can be achieved with much shorter time constants.

Digital Phase Shifting

Analog phase shifting circuits have also been replaced with a DSP calculation. Phase is measured with 0.01° resolution, and the X and Y outputs are orthogonal to 0.001°.

Frequency Synthesizer

The built-in direct digital synthesis (DDS) source generates a very low distortion (–80 dBc) reference signal. Single frequency sine waves can be generated from 1 mHz to 102 kHz with 4½ digits of resolution. Both frequency and amplitude can be set from the front panel or from a computer. When using an external reference, the synthesized source is phase locked to the reference signal.

Useful Features

Auto-functions allow parameters that are frequently adjusted to automatically be set by the instrument. Gain, phase, offset and dynamic reserve are quickly optimized with a single key press. The offset and expand features are useful when examining small fluctuations in a measurement. The input signal is quickly nulled with the auto-offset function, and resolution is increased by expanding around the relative value by up to 100×. Harmonic detection isn't limited to 2F—any harmonic (2F, 3F, ... nF) up to 102 kHz can be measured.

Analog Inputs and Outputs

Both instruments have a user-defined output for measuring X, R, X-noise, Aux 1, Aux 2, or the ratio of the input signal to an external voltage. The SR830 has a second, user-defined output that measures Y, θ, Y-noise, Aux 3, Aux 4 or ratio. The SR810 and SR830 both have X and Y analog outputs (rear panel) that are updated at 256 kHz. Four auxiliary inputs (16-bit ADCs) are provided for general purpose use—like normalizing the input to source intensity fluctuations. Four programmable outputs (16-bit DACs) provide voltages from –10.5 V to +10.5 V and are settable via the front panel or computer interfaces.

Internal Memory

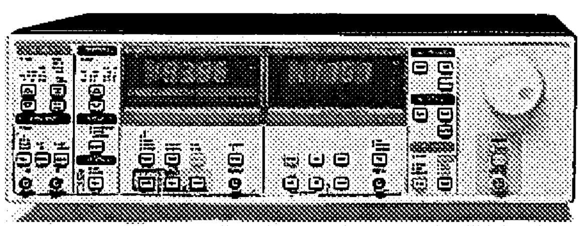
The SR810 has an 8,000 point memory buffer for recording the time history of a measurement at rates up to 512 samples/s. The SR830 has two, 16k point buffers to simultaneously record two measurements. Data is transferred from the buffers using the computer interfaces. A trigger input is also provided to externally synchronize data recording.

Easy Operation

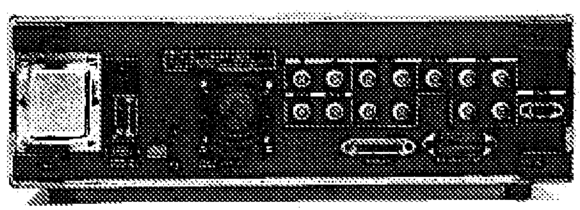
The SR810 and SR830 are simple to use. All functions are set from the front-panel keypad, and a spin knob is provided to quickly adjust parameters. Up to nine different instrument configurations can be stored in non-volatile RAM for fast and easy instrument setup. Standard RS-232 and GPIB (IEEE-488.2) interfaces allow communication with computers.

Ordering Information

SR830	DSP dual phase lock-in amplifier (w/ rack mount)	\$4500
SR810	DSP single phase lock-in amplifier (w/ rack mount)	\$3850
SR550	Voltage preamplifier (100 MΩ, 3.6 nV/√Hz)	\$595
SR552	Voltage preamplifier (100 kΩ, 1.4 nV/√Hz)	\$595
SR554	Transformer preamplifier (0.091 nV/√Hz)	\$995
SR540	Optical chopper	\$1095



SR810 DSP Single Phase Lock-In Amplifier



SR810/830 rear panel

Signal Channel

Voltage inputs	Single-ended or differential
Sensitivity	2 nV to 1 V
Current input	10^6 or 10^8 V/A
Input impedance	
Voltage	10 MΩ + 25 pF, AC or DC coupled
Current	1 kΩ to virtual ground
Gain accuracy	±1 % (±0.2 % typ.)
Noise (typ.)	6 nV/√Hz at 1 kHz 0.13 pA/√Hz at 1 kHz (10^6 V/A) 0.013 pA/√Hz at 100 Hz (10^8 V/A)
Line filters	50/60 Hz and 100/120 Hz (Q = 4)
CMRR	100 dB to 10 kHz, decreasing by 6 dB/oct above 10 kHz
Dynamic reserve	>100 dB (without prefilters)
Stability	<5 ppm/°C

Reference Channel

Frequency range	0.001 Hz to 102.4 kHz
Reference input	TTL or sine (400 mVpp min.)
Input impedance	1 MΩ, 25 pF
Phase resolution	0.01° front panel, 0.008° through computer interfaces
Absolute phase error	<1°
Relative phase error	<0.001°
Orthogonality	90° ± 0.001°
Phase noise	
Internal ref.	Synthesized, <0.0001° rms at 1 kHz
External ref.	0.005° rms at 1 kHz (100 ms time constant, 12 dB/oct)
Phase drift	<0.01°/°C below 10 kHz, <0.1°/°C above 10 kHz
Harmonic detection	2F, 3F, ... nF to 102 kHz (n < 19,999)
Acquisition time	(2 cycles + 5 ms) or 40 ms, whichever is larger

Demodulator

Stability	Digital outputs and display: no drift Analog outputs: <5 ppm/°C for all dynamic reserve settings
Harmonic rejection	−90 dB
Time constants	10 µs to 30 ks (6, 12, 18, 24 dB/oct rolloff). Synchronous filters available below 200 Hz.

Internal Oscillator

Range	1 mHz to 102 kHz
Frequency accuracy	25 ppm + 30 µHz
Frequency resolution	4½ digits or 0.1 mHz, whichever is greater
Distortion	−80 dBc (f <10 kHz), −70 dBc (f >10 kHz) @ 1 Vrms amplitude
Amplitude	0.004 to 5 Vrms into 10 kΩ (2 mV resolution), 50 Ω output impedance, 50 mA maximum current into 50 Ω
Amplitude accuracy	1 %
Amplitude stability	50 ppm/°C
Outputs	Sine, TTL (When using an external reference, both outputs are phase locked to the external reference.)

Displays

Channel 1	4½-digit LED display with 40-segment LED bar graph. X, R, X-noise, Aux 1 or Aux 2. The display can also be any of these quantities divided by Aux 1 or Aux 2.
Channel 2 (SR830)	4½-digit LED display with 40-segment LED bar graph. Y, θ, Y-noise, Aux 3 or Aux 4. The display can also be any of these quantities divided by Aux 3 or Aux 4.
Offset	X, Y, R can be offset up to ±105 % of full scale.
Expand	X, Y, R can be expanded by 10× or 100×.
Reference	4½-digit LED display

Inputs and Outputs

CH1 output	X, R, X-noise, Aux 1 or Aux 2, (±10 V), updated at 512 Hz
CH2 output (SR830)	Y, θ, Y-noise, Aux 3 or Aux 4, (±10 V), updated at 512 Hz
X, Y outputs (rear panel)	In-phase and quadrature components (±10 V), updated at 256 kHz.
Aux. A/D inputs	4 BNC inputs, 16-bit, ±10 V, 1 mV resolution, sampled at 512 Hz
Aux. D/A outputs	4 BNC outputs, 16-bit, ±10 V, 1 mV resolution
Sine out	Internal oscillator analog output
TTL out	Internal oscillator TTL output
Data buffer	The SR810 has an 8k point buffer. The SR830 has two 16k point buffers. Data is recorded at rates to 512 Hz and read through the computer interfaces.
Trigger in (TTL)	Trigger synchronizes data recording
Remote preamp	Provides power to the optional SR550, SR552 and SR554 preamps

General

Interfaces	IEEE-488.2 and RS-232 interfaces standard. All instrument functions can be controlled and read through IEEE-488.2 or RS-232 interfaces.
Power	40 W, 100/120/220/240 VAC, 50/60 Hz
Dimensions	17" × 5.25" × 19.5" (WHD)
Weight	23 lbs.
Warranty	One year parts and labor on defects in materials and workmanship